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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,191	08/03/2006	Darrell H. Reneker	089498.0449.US	2634

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EXAMINER	
BUCKLEY, AUDREA	
ART UNIT	PAPER NUMBER
1611	
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06/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,191	RENEKER ET AL.	
	Examiner	Art Unit	
	AUDREA J. BUCKLEY	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *15-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 35-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/4/2006 (2) and 1/10/2006 (1)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 15-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected methods of making and using, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/16/2010.

Applicant's election without traverse of Group I, claims 1-14 and 35-48, in the reply filed on 4/16/2010 is acknowledged.

Priority

This application is a 371 of PCT/US04/12673, filed 4/23/2004 which claims benefit of 60/464,879, filed 4/23/2003.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 1/4/2006 (2) and 1/10/2006 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 5, 6, 10, 11, 13, 35, 36, 39, 40, 41, 44, 45, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler et al. (US 6,232,434, patented May 2001).

Regarding claims 1, 2, 6, 35, and 36, Stamler et al. teach polymers for delivering nitric oxide in vivo (see abstract, in particular). These polymers include fiber forms of polymeric materials (see column 4, line 16). Specifically, a polymer having a “stabilized

S-nitrosyl group" is employed for nitric oxide (NO) release (see column 2, lines 9-15, in particular). As to claim 41, Stamler et al. teach that acid is added to react with a nitrite salt (see column 8, lines 4-5). Stamler et al. teach a variety of reasons for releasing nitric oxide in vivo including the treatment of medical conditions benefitting from the anti-inflammatory effects of nitric oxide on muscle tissue (see column 1, lines 28-36). Regarding claims 5, 10, 11, 39, 40, 44, 45, and 47, the nitric oxide is delivered to a bodily fluid, for example blood, by contacting the bodily fluid with a tube or catheter coated with one or more of the polymers of the disclosed invention (see column 3, lines 14-17). In the disclosure of Stamler et al., the bodily fluid which is blood acts as a solvent; that is, the blood plasma acts as a solvent, and, not being a polymer or fatty chain, the blood plasma solvent is a low molecular weight liquid as required by claim 13.

As to claim 1, Stamler et al. do not teach specifically that the embodiments of the invention necessarily employ a fiber form of the polymeric materials disclosed.

However, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize fibers as the reactive agent substrate. One would have been motivated to do so as suggested by Stamler et al. (see column 4, line 16), and one of ordinary skill in the art at the time the invention was made reasonably would have expected continued success based on the fiber format of the polymer employed to deliver the nitric oxide reactants to an in vivo application.

Claims 3, 4, 37, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler et al. (US 6,232,434, patented May 2001) as applied to

claims 1, 2, 5, 6, 10, 11, 13, 35, 36, 39, 40, 41, 44, 45, and 47 above, and further in view of Chu et al. (US 6,685,956 B2, filed May 2001, submitted in IDS of 1/4/2006).

The teachings of Stamler et al. are delineated above. Stamler et al. do not teach nanofibers in particular as fibers useful in the disclosed invention.

However, Chu et al. teach fibrous articles in medical applications wherein nano-scale fibers are used. Preferably, fibers having a diameter most preferably between 20 and 500 nanometers are used (see column 4, lines 36-44).

Although Chu et al. teach electrospinning for fiber formation, as to the preparation methodology in claims 4 and 38, it is noted that this is a product-by-process limitation which is not granted patentable weight, in accordance with MPEP 2113. The patentability of a product does not depend on its method of production; if the product in the product by process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process. See *In re Thorp,* 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use nano-scale fibers as taught by Chu et al. One would have been motivated to do so in order to implement the desirable feature of improved control over release properties, thereby facilitating fine tuning of the drug release rate (see column 7, lines 63-67).

Claims 7, 14, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler et al. (US 6,232,434, patented May 2001) as applied to

claims 1, 2, 5, 6, 10, 11, 13, 35, 36, 39, 40, 41, 44, 45, and 47 above, and further in view of Trescony et al. (US 5,994,444, patented Nov. 1999, submitted in IDS of 1/4/2006).

The teachings of Stamler et al. are delineated above. It is further pointed out that Stamler et al. teach that acid is added to react with a nitrite salt (see column 8, lines 4-5). Carboxylic acids are among those acceptable for this reaction (see column 4, line 64).

Stamler et al. do not teach an embodiment of the invention in which a carboxylic acid in particular is employed in the aforementioned reaction as required by claim 7; for this reason, this rejection is made using obviousness rationale. Stamler et al. do not teach that ascorbic acid (a carboxylic acid) reacts with nitrite as in pending claims 14 and 48.

However, Trescony et al. also teach a polymeric material that releases nitric oxide. The polymeric material is formed from a polymer matrix which is impregnated with a nitric oxide donor for release of nitric oxide upon hydration (see abstract, in particular). Specifically, Trescony teaches that the polymeric material includes a reducing functionality such as ascorbic acid or ascorbate (including esters containing ascorbic acid) so that this reducing functionality can donate one or more elections to the reduction of nitrite (NO_2^-) to nitric oxide (NO) (see column 5, lines 1-3 and lines 23-32).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine ascorbic acid with nitrite for the production of nitric oxide. One would have been motivated to do so based on the disclosure of

Trescony et al. which specifically teaches ascorbic acid as a reducing agent to be combined with nitrite for the successful production of nitric oxide from a polymeric material (see column 5, lines 66 – column 6, line 15).

Claims 8 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler et al. (US 6,232,434, patented May 2001) as applied to claims 1, 2, 5, 6, 10, 11, 13, 35, 36, 39, 40, 41, 44, 45, and 47 above, and further in view of Santerre et al. (US 5,798,115, patented Aug. 1998).

The teachings of Stamler et al are delineated above. This reference does not disclose the urethane prepolymer and diamine or diol as required in claim 8, nor does this reference teach one of these components as in claim 42.

However, Santerre et al. teach bioresponsive pharmacologically active polymers and articles made therefrom. The invention relates to polymeric compounds and substrates such as implantable medical devices formed from or coated with the pharmacologically active polymeric materials. Pharmacological agents are released in response to in vivo activation at a desired location in a mammal. The pharmacologically active compounds provide in vivo enhanced long term anti-inflammatory, anti-bacterial, anti-microbial, and/or anti-fungal activity (see abstract, in particular). In particular, Santerre et al. teach a diisocyanate (polyurethane prepolymer) reacting with a surface-activatied tubing material by reaction of free diisocyanates with active carboxylic acid, amine, or hydroxyl groups (see column 11, lines 25-30). For instance, in Example 4

(see column 16, lines 20-37), hexamethylene diisocyanate is reacted with Jeffamine-900 polyether diamine following addition of the active agent.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to react the diisocyanate (polyurethane prepolymer) with diamine as taught by Santerre et al. in the polymer devices of Stamler et al. One would have been motivated to do so since Santerre et al. teach that the pharmacologically active fragment is reacted from a polymeric backbone in in vivo applications benefitting from reduced incidence of infection due to the presence of access devices. One further would have been motivated to do so since the in vivo pharmacological activity may be for example, anti-inflammatory in nature (see column 6, lines 16-67).

Claims 9 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler et al. (US 6,232,434, patented May 2001) as applied to claims 1, 2, 5, 6, 10, 11, 13, 35, 36, 39, 40, 41, 44, 45, and 47 above, and further in view of Anand et al. ("Ion-exchange resins: carrying drug delivery forward", DDT Vol. 6, No. 17, September 2001).

The teachings of Stamler et al. are delineated above. Stamler et al. do not teach that a reactive component is bound to an ion-exchange resin bead as in pending claims 9 and 43.

However, Anand et al. teach that ion exchange resin beads are comprised of a structural component consisting of a polymer matrix and a functional component to

which the counter ion is bound (see page 906, end of first column). Specifically, these beads are applicable to drug delivery systems (see page 908, column 1, paragraph 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the ion exchange resin beads as taught by Anand et al. in the polymers for drug delivery as taught by Stamler et al. One would have been motivated to do so in order to improve the controlled- or sustained- release of drug dosage, particularly since Anand et al. teach that ion exchange resins impart desirable flexibility in designing drug delivery systems since these resins release the drug more uniformly than would a simple matrix (see page 908, column 1, paragraph 2).

Claims 12 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler et al. (US 6,232,434, patented May 2001) as applied to claims 1, 2, 5, 6, 10, 11, 13, 35, 36, 39, 40, 41, 44, 45, and 47 above, and further in view of Keefer et al. (US 5,650,447, patented Jul. 1997, submitted in IDS of 1/4/2006).

The teachings of Stamler et al. are delineated above. It is not apparent from this disclosure that one of the fibers necessarily dissolves or swells in the presence of a releasing agent as required by pending claims 12 and 46.

Keefer et al., however, teach the administration of nitric oxide by release from a polymeric material in order to deliver ameliorating, prophylactic, or therapeutic drug dosing for restenosis and related disorders (see abstract, in particular). Specifically, Keefer et al. explicitly teach that the polymer of the polymer-bound compositions may

dissolve in a physiological environment in order to desirably deliver the active agent (see column 9, lines 5-7).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to employ the polymer dissolution feature as taught by Keefer et al. One would have been motivated to do so in order to impart the biodegradable feature as taught by Keefer et al., thereby eliminating the need for fiber removal post delivery of the bioactive agent.

Conclusion

No claims are found allowable at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AUDREA J. BUCKLEY whose telephone number is (571)270-1336. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/AJB/

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611